Remarks

Substitute drawing sheets are being submitted herewith in accordance with MPEP §§608.02(h) and 608.02(v) to correct obvious errors. In the preliminary amendment submitted by Applicants on January 11, 2002, the subscripts in Figure 1 were clarified. However, the letter "A" was inadvertently omitted in the corrected substitute drawing sheet. The corrections would be obvious to one of skill in the art, and the clarification is supported, for example, in Rajagopalan et al., *Biochemistry*, 36:13910-18 (1997), which was cited on page 24, lines 17-18 of the present application and incorporated by reference at page 64, lines 32-35 of the present application. In Figure 10, sequence i.d. labels are being added to the illustrated sequences.

The specification has also been amended to add sequence i.d. labels.

Conclusion

The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number, if there are any questions regarding this Preliminary Amendment or if prosecution of this application may be assisted thereby.

Respectfully submitted for

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APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/896,580
Docket No.: 6317.N

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

The paragraph beginning at **page 12, line 28**, has been amended as follows:

Figure 10 is a sequence alignment based on x-ray structure comparisons for *E. coli* pdf (SEQ ID NO:8) and *S. aureus* pdf (SEQ ID NO:7) proteins.

The paragraph beginning at **page 25, line 18**, has been amended as follows:

S.aureus pdf has seven insertions with respect to the *E.coli* sequence (Figure 10). The first insertion T3-M4 adds some additional hydrophobic surface area which forms a small surface for interaction with the third insertion (the extended n-terminal helix) N43-G54. The insertion after P25 adds one additional residue to the turn, which leads into the first long helix of pdf. This n-terminal helix is extended by an additional helix (insertion three N43-G54) which is not present in the *E.coli* structure. In the *E.coli* structure this helix is followed by a beta turn which drops down into the very conserved GXGLAA (SEQ ID NO:9) sequence which forms the third (and edge) strand of the n-terminal β-sheet. This strand also forms part of the wall of the active site crevice and provides loci for hydrogen bonding of peptide substrates (Hao et al., *Biochemistry*, 38: 4712-19 (1999)). The insertion of residues G81-G83 in the *S.aureus* structure extends the turn between strands II and III of the n-terminal β-sheet. The insertion of V100 is in the turn between strand I of the central anti-parallel β-sheet and the central strand of the c-terminal mixed sheet. Insertion six occurs at the end of the central strand of the mix sheet and includes P106 and T107. These residues are positioned at the opening of the active site crevice and may be important determinates of *S.aureus* specificity. The subsequent conserved residues EGCLS (SEQ ID NO:10) form the other wall of the active site crevice. Residue C111 at the center of this sequence is one of the active site metal ligands. The conserved glutamic acid projects downward to form a part of the crevice wall and makes a conserved salt bridge with

R124, which is found in the center of the first strand of the mix β-sheet. The insertion of A119 results in a slight bulge of the connecting strand (with respect to the *E.coli* structure) which precedes the first strand of the c-terminal mixed β-sheet. This seventh insertion, the sixth insertion (P106/T107) [both located in the thumb] and the c-terminal extension are all in close proximity and constitute a *S.aureus* specific surface.

The paragraph beginning at **page 28, line 7**, has been amended as follows:

Comparison of the *E.coli* and *S.aureus* crystal structures indicates that six residues in the region of the active site are conserved. In fact, five are always conserved in pdf sequences (ETB, data not shown). The residues come from the three regions of greatest sequence identity; Gxglaa (SEQ ID NO:9), EGCls (SEQ ID NO:10), and IxxqHexdhl (SEQ ID NO:11), where the capitization indicates a conserved residue in the active site crevice. The first glycine is the lone invariant amino acid on the right side of the cleft (Figure 15). The glutamic-glycine-cysteine triplet forms the invariant left side of the crevice. Finally, isoleucine and histidine are found at the bottom of the active site crevice (Figure 15). These conserved residues form a continuous invariant surface which extends from the methionine (caproyl) site (S1) and up the left wall of the crevice. The variable residues encircle the upper aspect of the crevice. The differences account for the subtle differences in crevice shape when the two enzymes are compared---and presumably will be important determinates for inhibitor specificity.

The paragraph beginning at **page 65, line 5**, has been amended as follows:

SEQUENCE LISTING FREE TEXT

SEQ ID NO:1 *Staphylococcus aureus* peptide deformylase with C-terminal 6xHis tag

SEQ ID NO:2 *Escherichia coli* peptide deformylase

SEQ ID NO:3 *Haemophilis influenzae* peptide deformylase

SEQ ID NO:4 *Bacillus subtilis* peptide deformylase

SEQ ID NO:5 *Mycoplasma pneumoniae* peptide deformylase

SEQ ID NO:6 *Staphylococcus aureus* defl gene (Pseudo pdf)

SEQ ID NO:7 *Staphylococcus aureus* peptide deformylase

SEQ ID NO:8 *Escherichia coli* peptide deformylase

SEQ ID NO:9 Amino Acid Residue

SEQ ID NO:10 Amino Acid Residue

SEQ ID NO:11 Amino Acid Residue